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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/655,588	09/05/2003	Willy Lagwinski	PP-19681.002	7324

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EXAMINER	
SINES, BRIAN J	

ART UNIT	PAPER NUMBER
1743	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/655,588	LAGWINSKI ET AL.	
	Examiner	Art Unit	
	Brian J. Sines	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *18-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group I comprising claims 1 – 17 in the reply filed on 3/6/2007 is acknowledged. The traversal is on the ground(s) that all of the methods are related in that they each utilize luminescent semiconductor nanocrystals and that there would be no undue burden on the examiner to examine all of the inventions together. This is not found persuasive because each of the inventions are indeed considered independent and distinct, since each invention has different modes of operation, or method steps, and resulting effects or purposes as is also indicated by the preambles to the base claims for each invention. For example, the method of invention 1, as recited in claim 1, is directed to a method for verifying the transfer of fluid from a first composition to a second composition. Whereas the method of invention 2 , as recited in claim 18, is directed to a method for monitoring the flow of a reagent. The method of invention 2 does not specifically require the use of a first and second composition as is required by the method of invention 1. The method of invention 1 does not involve the monitoring of the flow of a reagent nor does invention 1 require a specific reagent other than the use of the luminescent semiconductor nanocrystals. Therefore, the methods of inventions 1 and 2 have different modes of operation or steps and different effects as is also indicated by their respective preambles in their independent base claims. The method of invention 3, as recited in claim 26, is directed to a method for verifying the transfer of a plurality of fluids to a container. The method of invention 3 involves the use of differing amounts of the semiconductor nanocrystals. Whereas the other methods do not employ nor specifically require this method step. The method of invention 4, as recited in claim 31, is directed to a method for

preparing a dilute solution. The method of invention involves a dilution step and the use of a predetermined dilution ratio. Whereas the other methods do not employ nor require this step. The method of invention 5, as recited in claim 32, is directed to a method for determining the cleanliness of a reaction vessel. This method specifically requires a step for cleaning a reactor vessel. Whereas the other methods clearly do not specifically employ or require this cleaning step. On page 2 in the second paragraph of the filed response to the restriction election requirement, the applicant similarly recognizes that although all of the claimed methods employ the use of luminescent semiconductor nanocrystals, each of the methods monitor the nanocrystals in "slightly different fashions," or *different modes of operation or steps*, to "slightly different ends," or *different effects*. The examiner agrees with this recognition and that is why the restriction election requirement was made. The issue that all of the methods involve the use of the luminescent semiconductor nanocrystals is not necessarily sufficient to require the withdraw of the restriction requirement since each of the methods involve different methodologies. Furthermore, the primary classification of the claimed subject matter is merely one indication of the burdensome nature of the search requirements and a serious burden on the examiner may also be shown by appropriate explanation of the field of search (see MPEP § 803). The restriction requirement merely refers to the primary classification for the inventions, not the complete scope of the prior art search in additional art class and subclass classifications that would be required in determining patentability. Clearly, since the different claim sets comprising each of the inventions comprise different methodologies, different searches and patentability determination issues are involved in the examination of each invention. The requirement is still deemed proper and is therefore made FINAL. Claims 18 – 36 are withdrawn from further consideration pursuant

to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 – 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 – 17 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are:

1. Regarding claim 1, the claimed method is incomplete. As indicated in the preamble, this claim is directed to a method for verifying the transfer of fluid from a first composition to a second composition. However, claim 1 does not positively recite a verification step for verifying the transfer of fluid from a first composition to a second composition. Are the luminescent semiconductor nanocrystals detected and quantified in the third composition to verify the delivered amount of the second composition into the first composition to form the third composition? Furthermore, the claim preamble and the recited method steps do not appear to correspond with one another. As recited in the third step of claim 1, it is the second composition that is transferred into the first composition to form a third composition. The preamble to claim 1 indicates that the first composition is transferred to or into the second composition. Claim 2 also indicates that it is the second composition that is transferred into the first composition.

2. Claim 15 recites the limitation "said second fluid" in line 3. There is insufficient antecedent basis for this limitation in the claim. The claim appears to be referring to the second composition in claim 1.

3. Regarding claim 15, it is unclear as to how the use of a nanocrystal linked to a target pertains to verifying the transfer of fluid. With respect to claim 1 to which claim 15 depends, does the applicant intend to mean a fluid having a first composition containing a detectable substance? Is the method directed to a method of assaying for an analyte that binds with the target linked to the semiconductor nanocrystal?

4. Regarding claim 16, the step of nucleic acid testing is unclear. How is the step of nucleic acid testing relate to the claimed method of verifying the transfer of fluid from a first composition to a second composition? Does the step involve determining of whether and how much of an addition product is present in a subsequent processing step or product? It is unclear as to how the nucleic acid testing step involving the luminescent semiconductor nanocrystals is performed. Does the amount of nanocrystals present verify the actual concentration of a nucleic acid component relative to previous concentration conditions in a time synchronous or non-synchronous replicate prior to amplification? Are the nanocrystals linked to a target nucleic acid to facilitate this verification?

5. Regarding claim 17, the use of the recited nanomolar nanocrystal concentration is unclear. It is unclear as to which composition contains the recited concentration. Is the recited nanomolar concentration of nanocrystals the initial concentration in the second composition before the transfer occurs, or in the final resulting mixture comprising the third composition in the method in claim 1?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 – 9 and 11 – 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Weiss et al. (U.S. Pat. No. 5,990,479 A) ("Weiss").

Regarding claims 1, 2 and 15, as disclosed by Weiss, the claimed methodology reads on a method for determining the presence of a detectable substance in a sample via a luminescent semiconductor nanocrystal probe (see, e.g., col. 2, line 16 – col. 3, line 29; col. 3, line 50 – col. 4, line 45; col. 10, line 25 – col. 11, line 8).

Weiss anticipates the steps of:

a. providing a first composition having a first fluid therein, e.g., a biological sample fluid material containing a detectable substance;

b. providing a second composition having a second fluid therein, wherein the second composition includes a predetermined amount of luminescent semiconductor nanocrystal capable of emitting electromagnetic radiation in a narrow wavelength band when excited, e.g. a second fluid contaning an organo-luminescent semiconductor nanocrystal probe linked with an affinity molecule;

c. transferring or contacting all or a portion of the second composition containing the nanocrystal probe into the first composition containing the detectable substance, thereby

forming a mixture or third composition (Note that the claimed method does not exclude a rinsing step for removing portions of nanocrystal probe material not bound to the detectable substance);

d. exposing the third composition to electromagnetic energy capable of exciting the nanocrystal probe material; and

e. then detecting the electromagnetic radiation energy emitted from the nanocrystals in the third mixture composition, whereby the amount of nanocrystal material and subsequently the amount of detectable substance can be quantified.

Therefore, the method disclosed by Weiss would verify or indicate the transfer or mixture of a fluid of a first composition, e.g., a sample fluid containing a detectable substance to which the nanocrystal probe material binds, to a second composition, e.g., a fluid composition containing both a detectable substance and the bound nanocrystal probe material.

Regarding claim 3, Weiss anticipates a nanocrystal having a core/shell structural configuration (see, e.g., col. 6, lines 17 – 34).

Regarding claims 4 and 5, Weiss anticipates a typical nanocrystal cross-section or diameter of 1 nm to 10 nm (see col. 4, lines 46 – 58).

Regarding claims 6 – 9, Weiss anticipates the use of CdS, CdSe, and ZnS, in making the nanocrystals (see col. 5, line 60 – col. 6, line 4).

Regarding claims 11 and 12, Weiss anticipates a nanocrystal core diameter of 20 to 100 Angstroms (2 – 10 nm) (see col. 6, lines 5 – 34).

Regarding claims 13 and 14, Weiss anticipates the incorporation of a nanocrystal shell, i.e., a thin layer of silica glass, having a thickness of about 0.5 nm to about 10 nm (see col. 7, lines 49 – 53; col. 6, lines 5 – 34).

Regarding claims 15 and 16, Weiss anticipates that the semiconductor nanocrystal probe can be linked to a target or affinity molecule present in the second fluid, such as antibodies or nucleic acids to facilitate nucleic acid testing (see col. 6, line 51 – col. 7, line 4).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 1 – 9 and 11 – 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weiss.

Regarding claims 1, 2 and 15, as disclosed by Weiss, the claimed methodology reads on a method for determining the presence of a detectable substance in a sample via a luminescent semiconductor nanocrystal probe (see, e.g., col. 2, line 16 – col. 3, line 29; col. 3, line 50 – col. 4, line 45; col. 10, line 25 – col. 11, line 8).

Weiss teaches the steps of:

a. providing a first composition having a first fluid therein, e.g., a biological sample fluid material containing a detectable substance;

b. providing a second composition having a second fluid therein, wherein the second composition includes a predetermined amount of luminescent semiconductor nanocrystal capable of emitting electromagnetic radiation in a narrow wavelength band when excited, e.g. a second fluid containing an organo-luminescent semiconductor nanocrystal probe linked with an affinity molecule;

c. transferring or contacting all or a portion of the second composition containing the nanocrystal probe into the first composition containing the detectable substance, thereby forming a mixture or third composition (Note that the claimed method does not exclude a rinsing step for removing portions of nanocrystal probe material not bound to the detectable substance);

d. exposing the third composition to electromagnetic energy capable of exciting the nanocrystal probe material; and

e. then detecting the electromagnetic radiation energy emitted from the nanocrystals in the third mixture composition, whereby the amount of nanocrystal material and subsequently the amount of detectable substance can be quantified.

Therefore, it would have been obvious to a person of ordinary skill in the art to utilize the method disclosed by Weiss to verify or indicate the transfer or mixing and subsequent detection of a fluid of a first composition, e.g., a sample fluid containing a detectable substance to which the nanocrystal probe material binds, to a second composition, e.g., a fluid composition containing both a detectable substance and the bound nanocrystal probe material.

Regarding claim 3, Weiss teaches a nanocrystal having a core/shell structural configuration (see, e.g., col. 6, lines 17 – 34).

Regarding claims 4 and 5, Weiss teaches a typical nanocrystal cross-section or diameter of 1 nm to 10 nm (see col. 4, lines 46 – 58).

Regarding claims 6 – 9, Weiss teaches the use of CdS, CdSe, and ZnS, in making the nanocrystals (see col. 5, line 60 – col. 6, line 4).

Regarding claims 11 and 12, Weiss teaches a nanocrystal core diameter of 20 to 100 Angstroms (2 – 10 nm) (see col. 6, lines 5 – 34).

Regarding claims 13 and 14, Weiss teaches the incorporation of a nanocrystal shell, i.e., a thin layer of silica glass, having a thickness of about 0.5 nm to about 10 nm (see col. 7, lines 49 – 53; col. 6, lines 5 – 34).

Regarding claims 15 and 16, Weiss teaches that the semiconductor nanocrystal probe can be linked to a target or affinity molecule present in the second fluid, such as antibodies or nucleic acids to facilitate nucleic acid testing (see col. 6, line 51 – col. 7, line 4).

2. Claims 10 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weiss in view of Bruchez et al. (U.S. Pat. No. 6,274,323 B1) ("Bruchez").

Regarding claim 10, Weiss does not specifically teach the use of monodisperse semiconductor nanocrystals.

Bruchez teaches the use of monodisperse semiconductor nanocrystals as detectable labels (see col. 9, lines 58 – 64). Consequently, as indicated by Bruchez, a person of ordinary skill in the art would accordingly have had a reasonable expectation for success of incorporating

the use of monodisperse semiconductor nanocrystals in the disclosed method. The prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success (see MPEP § 2143.02). Therefore, it would have been obvious to a person of ordinary skill in the art to incorporate the use of monodisperse semiconductor nanocrystals with the disclosed method to facilitate effective sample fluid processing, detection and quantification.

Regarding claim 17, Weiss does not specifically teach the recited nanocrystal nanomolarity.

Bruchez does teach the use of a 0.75 nanomolar concentration of semiconductor nanocrystals for use in an assay (see col. 48, lines 19 – 53). Consequently, the nanomolar concentration of semiconductor nanocrystals used can be considered a known result-effective variable that can be determined by a person of ordinary skill in the art without undue experimentation. Therefore, it would have been obvious to a person of ordinary skill in the art to incorporate the use of the recited nanomolar concentration of semiconductor nanocrystals as claimed.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The additional cited prior art teach methods of using semiconductor nanocrystals to detect and track various materials.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Sines whose telephone number is (571) 272-1263. The examiner can normally be reached on Monday - Friday (11 AM - 8 PM EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brian J. Sines
Primary Examiner
Art Unit 1743